REMARKS

I. Status of the Application

Claims 1-3, 5 and 6 are pending in the application. New claims 13-15 have been added. Applicants gratefully acknowledge that claims 1 and 2 have been indicated by the Examiner to be free from the prior art (page 7 of the final Office Action). Claim 3 is objected to because of various informalities. Claims 3, 5 and 6 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite. Claims 3 and 5 remain rejected under 35 U.S.C. § 103(a) as being unpatentable over Keung et al. Claims 3, 5 and 6 remain rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-6 of U.S. Patent No. 5,624,910. Claims 3, 5 and 6 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,204,369 or U.S. Patent No. 5,624,910.

Applicants have amended the claims to more clearly define and distinctly characterize Applicants' novel invention. Support for the amendments can be found in the specification and the claims as originally filed. Support for claim 3 to recite amino derivatives of tetroses, pentoses, or heptoses, alcohol derivatives of tetroses, pentoses, or heptoses, acid derivatives of tetroses, pentoses, or heptoses and deoxy analogs of tetroses, pentoses, or heptoses can be found at least at page 11, lines 2-5. Support for new claims 13-15 can be found in claims 3, 5 and 6, respectively, as originally filed. Support for an aldehyde that is 5-hydroxyindole-3-acetaldehyde or 3,4-dihydroxyphenyl-3-acetaldehyde as recited in claim 15 can be found at least at page 10, lines 11-13. Claim 2 was amended to correct an inadvertent typographical error.

The amendments presented herein add no new matter. Applicants respectfully request entry and consideration of the foregoing amendments and remarks, which are intended to place this case in condition for allowance.

II. Objection to Claim 3

At page 3, paragraph 6 of the final Office Action, claim 3 is objected to due to various informalities. Without acquiescing to the Examiner's objection, Applicants respectfully submit that claim 3 has been amended to recite proper Markush terminology and to replace "and" with "or" between "L" and "D" and between "aldo-" and "keto-," thus obviating the Examiner's objection.

III. Claims 3, 5 and 6 Are Definite

At page 4, paragraph 1 of the final Office Action, claims 3, 5 and 6 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. The Examiner asserts that the term "biogenic" renders the claim vague and indefinite because the Examiner is unable to locate in Applicants' specification what is meant or embraced by the term "biogenic" aldehyde.

Applicants respectfully traverse the rejection as Applicants believe that the term biogenic is well understood by those of skill in the art. However, Applicants have amended claims 3 and 6 to remove the term in order to facilitate allowance of the application. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

IV. Claims 3 and 5 and New Claims 13-15 are Patentable Over Keung et al.

At page 2, paragraph 8 of the final Office Action, claims 3 and 5 remain rejected under 35 U.S.C. § 103(a) as being unpatentable over Keung et al. The Examiner states that it is Applicants' position that the Keung et al. reference does not disclose the claimed compounds containing non-glucose sugar moieties. The Examiner asserts that claim 3 sets forth that "R" may be a "hexose," which encompasses the "glucose" moiety of daidzin. The Examiner concludes that Keung et al. claims daidzin, which continues to be embraced by claim 3. Applicants respectfully traverse this rejection based on the amended claims now presented.

Claim 3 has been amended to exclude hexoses, and new claims 13-15 do not recite sugar moieties. As amended, claim 3 recites substituents in the R position which are a non-glucose sugar moiety, a peptide, a polyether or an aminoalkyl. New claims 13-15 recite substituents in the R position which are a peptide, a polyether or an aminoalkyl. Keung et al. neither teaches nor suggests Applicants' claimed compounds. Accordingly, Applicants respectfully request the rejection of claims 3 and 5 as being obvious under 35 U.S.C. § 103(a) in view of Keung et al. be reconsidered and withdrawn.

V. Rejection of Claims 3, 5 and 6 Under Obviousness-Type Double Patenting

At page 2, paragraph 8 of the final Office Action, claims 3, 5 and 6 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-

6 of U.S. Patent No. 5,624,910 (the '910 patent). The Examiner states it is Applicants' position that the '910 patent does not disclose the claimed compounds containing non-glucose sugar moieties. The Examiner asserts that claim 3 sets forth that "R" may be a "hexose," which encompasses the "glucose" moiety of daidzin. The Examiner concludes that the '910 patent claims daidzin, which continues to be embraced by claim 3. Applicants respectfully traverse this rejection based on the amended claims now presented.

Applicants have amended the claims to exclude hexoses from the compounds of formula I. As amended, claim 3 recites substituents in the R position which are a non-glucose sugar moiety, a peptide, a polyether or an aminoalkyl. New claims 13-15 recite substituents in the R position which are a peptide, a polyether or an aminoalkyl. Claims 1-6 of the '910 patent do not disclose the compounds of amended claim 3 or of new claims 13-15, nor do claims 1-6 disclose the use of Applicants' claimed compounds in a method of therapeutically reducing alcohol consumption in a human in need thereof. Thus claims 1-6 of the '910 patent neither teach nor suggest all of Applicants' claim limitations. Accordingly, Applicants respectfully request that this obviousness-type double patenting rejection of claims 3, 5 and 6 be reconsidered and withdrawn.

VI. Claims 3, 5 and 6 and New Claims 13-15 Are Patentable Over U.S. Patent Nos. 5,204,369 and 5,264,910

At page 5, paragraph 3 of the final Office Action, claims 3, 5 and 6 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,204,369 (the '369 patent) or the '910 patent. The Examiner asserts that it would have been obvious to one of ordinary skill in the art at the

time the invention was made to modify the alcohol dependence treatment of the '369 patent to administer the daidzin derivatives disclosed by the '369 patent and the '910 patent because one of ordinary skill in the art would be able to determine the preferred derivatives useful in the treatment of alcohol dependence. Regarding claim 6, the Examiner is of the opinion that since the '369 patent and the '910 patent disclose administration of substantially similar active agents, i.e., daidzin and derivatives thereof, to a host, i.e., a human, using Applicants' claimed method steps to increase concentrations of the aldehydes in claim 6 would have been obvious. Applicants respectfully traverse these rejections.

Applicants' methods are based on the discovery that Applicants' claimed compounds cause the accumulation of aldehydes formed during catabolism of a neurotransmitter. Such aldehydes include 5-hydroxyindole-3-acetaldehyde (5-HIAL) and 3,4-dihydroxyphenyl-3-acetaldehyde (DOPAL), reactive intermediates of the serotonin and dopamine pathways, respectively (page 10, lines 11-13 and 21-25). Applicants' have discovered a linear correlation between 5-HIAL and DOPAL accumulation and ethanol intake suppression (page 18, lines 12-18; page 19, lines 2-8; and Figures 1-3). Thus, Applicants have discovered a mechanistic basis for reducing alcohol consumption (page 19, lines 5-8).

Applicants respectfully submit that the '369 and '910 patents neither teach nor suggest therapeutically reducing alcohol consumption by administering a compound in an effective amount ***to increase*** the concentration of an ***aldehyde formed during catabolism of a neurotransmitter***, as claimed by Applicants. The '369 and '910 patents are primarily concerned with inhibiting ALDH-I. The goal of the '910 patent is to identify ALDH-I inhibitory compounds and compositions (see

abstract). Both patents teach that "ALDH-I is present in mitochondria, has a high affinity for acetaldehyde, and has been assigned the ***major role in acetaldehyde detoxification***. ALDH-II, on the other hand, occurs in the cytosol and has a low affinity for acetaldehyde. It is therefore thought to be ***less effective in its detoxification***." (column 5, lines 25-30, '910 patent; column 5, lines 25-29, '369 patent, emphasis added). These references go on to teach that "since the lack of ALDH-I is not known to generate other significant metabolic problems, save those which are a consequence of ethanol metabolism, it would be ideal if a drug could be found which mimics the effect of this natural genetic variant..." (column 6, lines 3-9, '910 patent; column 6, lines 5-10, '369 patent). Thus, the patents are concerned with modifying alcohol consumption via the inhibition of ALDH-I.

The '369 and '910 patents are silent regarding increasing the concentration of an aldehyde formed during catabolism of a neurotransmitter, and provide no evidence that inhibiting ALDH-I could function to increase the concentration of any aldehyde formed during catabolism of a neurotransmitter. Although the '369 and '910 patents teach inhibiting ALDH-I, such an inhibition would merely serve to increase the levels of the aldehyde CH_3CHO (i.e., acetaldehyde) in the body (see, for example, column 1, lines 55-63 the '369 patent). Acetaldehyde is not an aldehyde that is formed during catabolism of a neurotransmitter.

In contrast, Applicants claim increasing the concentration of an aldehyde formed during catabolism of a neurotransmitter using the claimed compounds. Applicants teach that aldehydes formed during catabolism of a neurotransmitter include 5-HIAL and DOPAL, and that ALDH-II is involved in neurotransmitter catabolism (page 9, lines 1-8). The '369 and '910 patents do not teach the involvement of ALDH-I in either of these pathways or in ***any*** pathway involving any aldehyde

formed during catabolism of a neurotransmitter. Thus, one of skill in the art, based on the teachings of the '369 patent or the '910 patent would not look to increase the level of an aldehyde formed during catabolism of a neurotransmitter as a method of reducing alcohol consumption.

Regarding new claims 13-15, Applicants respectfully submit that in addition to failing to teach increasing the level of an aldehyde formed during catabolism of a neurotransmitter, neither the '369 patent nor the '910 patent teach or suggest the compounds of Applicants' claimed method. The '369 patent teaches daidzin and synthetic derivatives of daidzin where the glucose moiety is replaced with a different sugar moiety (column 14, lines 1-8). The '910 patent teaches daidzin and synthetic derivatives of daidzin where the glucose moiety is replaced with a different sugar moiety, or where the glucose moiety is replaced by alkoxy or acyloxy groups (column 13, lines 40-57). Claims 13-15 recite only peptide, polyether or aminoalkyl substituents in the R position. Claims 13-15 do not recite a sugar moiety or alkoxy or acyloxy groups. Neither of the patents cited by the Examiner teaches or suggests Applicants' claimed compounds.

VII. CONCLUSION

Reconsideration and allowance of all the pending claims is respectfully requested. If a telephone conversation with Applicants' attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 720-9600.

Respectfully submitted,

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